PHOSPHITE MANUFACTURERS CONSORTIUM (PMC)
RESPONSE TO EPA COMMENTS ON THE US HPV CHALLENGE SUBMISSION FOR
TRIS (NONYLPHENYL) PHOSPHITE (TNPP, CAS NO. 26523-78-4)

November 15, 2006

The following is intended to provide an official response to EPA's October 2000 comments on the robust summaries and test plan submitted for tris (nonylphenyl) phosphite (TNPP, CAS No. 26523-78-4). With this response, the sponsor (Phosphite Manufacturers Consortium, PMC) considers its HPV commitment complete for this substance.

Attachment I provides robust summaries in a IUCLID style format. As you are likely aware, TNPP is listed on the EU 4th Priority List and industry has been actively working over the last several years with the EU authorities, specifically France's INRS (Institut National de Recherche et de Sécurité), INERIS (Institut National de l'Environnement Industriel et des Risques) and BERPC (Bureau d'Évaluation des Risques des Produits et agents Chimiques), to develop a complete dossier for TNPP. As such, Attachment I contains information beyond what is required by the US HPV Challenge Program (and includes what was already provided in our September 2001).

Excerpts from EPA's comments are provided below in *italicized Arial* text, followed by the sponsor's indented response.

Chemical characterization

A brief statement of the uses of the chemical would help reviewers assess the appropriateness of some of the proposed tests.

> We have added a brief description of the uses of TNPP to Section 1.7 of Attachment I.

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient)

Data were submitted for vapor pressure. The sponsor's approach for the remaining endpoints should satisfy the needs of the U.S. HPV Challenge Program.

> New studies were conducted and are summarized in Attachment I.

Fate (photodegradation, stability in water, biodegradation, and transport/distribution)

EPA believes the sponsor's approach should satisfy these endpoints. However, the test plan does not specify the model to be used for transport/distribution estimation. EPA prefers the EQC Level III fugacity model (available free from http://www.trentu.ca/academic/aminss/envmodel/) for the U.S. HPV Challenge Program.

> Level III fugacity modeling was conducted, the results of which are summarized in Attachment I.

Ecological Effects – Acute Aquatic Toxicity

Robust summaries were submitted for acute studies on fish, daphnia, and green algae (one study summary for each organism). The submitted test data for fish, daphnia, and green algae could not be adequately evaluated because of the following deficiencies in reporting:

1) *The composition of the test material was not reported. The material was identified only by product name with no analytical data.*

2) *The predicted log P value of 20 indicates a much lower water solubility than the reported EC50. Information on the preparation of stock solution was not given, such as use of a carrier solvent, and whether it was determined that the substance was dissolved and not merely dispersed.*

EPA reserves further comment on these studies pending results of the planned water solubility testing.

New studies have been conducted and are summarized in Attachment I.

Health Effects – Acute Toxicity

There were three robust summaries submitted for acute oral toxicity. The first two (Unpublished, 1957, 1965) appear to have enough information to be considered adequate in the U.S. HPV Challenge Program, whereas the other (Majlathova, 1981) is missing important information (number of animals, doses used, strains of rat/mouse used, observation period).

Because adequate summaries were submitted for acute oral toxicity, EPA believes no further acute toxicity studies are needed for the purposes of the U.S. HPV Challenge Program.

Per EPA's comment, no further acute toxicity testing was conducted.

Health Effects – Repeat dose toxicity

Sufficient information has been provided for this endpoint. Therefore, there is no need to perform the proposed combined repeat dose/reproductive/developmental toxicity screening test (OECD Test Guideline 422). An alternative is to conduct the combined reproductive/developmental toxicity screening test (OECD Test Guideline 421).

A modified OECD 421 test was conducted and is summarized in Attachment I.

Health Effects – Genotoxicity

EPA's position is that the robust summary submitted for this endpoint [Salmonella assay] is not adequate for the purposes of the U.S. HPV Challenge Program [see next paragraph] and so there is a need to repeat the study. In addition, the sponsor is proposing to conduct an in vivo genotoxicity study which is beyond the needs of the U.S. HPV Challenge Program. The sponsor presented no rationale for conducting the in vivo genotoxicity study.

A new Salmonella assay was conducted according to OECD 471 and is summarized in Attachment I. Per EPA's comment, in vivo genotoxicity testing was conducted.

Health Effects – Reproductive Toxicity

The sponsor included a robust summary of the two-year rat study described above in the repeat dose toxicity section. This study had a reproductive toxicity component in its design, however, there was not enough information in the robust summary to consider it adequate for this endpoint in the U.S. HPV Challenge Program. The following information was not presented: (1) methodology related to the reproductive toxicity portion of the test; (2) the premating, mating, and postmating dosing regimen; (3) method of determining proof of pregnancy; (4) the exact number of animals that were pregnant and gave birth, and the associated number of pups; (5) how mating occurred to produce the second generation of offspring; and (6) detailed results by generation.

A modified OECD 421 test was conducted and is summarized in Attachment I.

Health Effects – Developmental Toxicity

The proposal includes conducting a combined repeat dose/reproductive/developmental toxicity screening test (OECD Test Guideline 422) in addition to a pre-natal developmental toxicity test (OECD 414). There is no rationale presented for conducting both tests. The OECD 421 screening study identified above is sufficient to cover the reproductive and developmental toxicity endpoints for the purposes of the U.S. HPV Challenge Program.

A summary of an in-vitro developmental toxicity study with chick embryos was presented. The study is not adequate or relevant to this endpoint for the U.S. HPV Challenge Program.

A modified OECD 421 test was conducted and is summarized in Attachment I.